AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

What is claimed is:

1. (Original) An isolated human antibody or fragment thereof that specifically binds to insulin-like growth factor-I receptor (IGF-IR) and has at least one property selected from the group consisting of

   (i) inhibits binding of IGF-I or IGF-II to IGF-IR;

   (ii) neutralizes activation of IGF-IR by IGF-I or IGF-II;

   (iii) reduces IGF-IR surface receptor by at least about 80%; and

   (iv) binds to IGF-IR with a K_d of about 3×10^{-10} M^{-1} or less.

2. (Original) The antibody or antibody fragment of Claim 1, which has all of said properties.

3. (Original) The antibody or antibody fragment of Claim 1, wherein the antibody or antigen binding fragment thereof reduces surface IGF-IR by at least about 85%.

4. (Original) The antibody or antibody fragment of Claim 1, wherein the antibody or antigen binding fragment thereof reduces surface IGF-IR by at least about 90%.

5. (Original) The antibody or antibody fragment of Claim 1, which binds to IGF-IR with a K_d of about 1×10^{-10} M^{-1} or less.

6. (Original) The antibody or antibody fragment of Claim 1, which binds to IGF-IR with a K_d of about 5×10^{-11} M^{-1} or less.

7. (Original) The antibody or antibody fragment of Claim 1, which inhibits phosphorylation of a downstream substrate of IFG-IR.

8. (Original) The antibody or antibody fragment of Claim 7, wherein the downstream substrate is selected from the group consisting of MAPK, Akt, and IRS-2, and phosphorylation is inhibited by about 50% or more.

9. (Original) The antibody or antibody fragment of Claim 1, which promotes tumor regression *in vivo*.

10. (Original) The antibody or antibody fragment of Claim 1, which promotes tumor regression *in vivo* when administered with an anti-neoplastic agent.

11. (Original) The antibody or antibody fragment of Claim 1, which competes for binding to IGF-IR with an antibody selected from the group consisting of

the antibody having a heavy chain variable domain represented by SEQ ID NO:2 and a light chain variable domain represented by SEQ ID NO:6; and

the antibody having a heavy chain variable domain represented by SEQ ID NO:2 and a light chain variable domain represented by SEQ ID NO:10.

12. (Currently Amended) The antibody or antibody fragment of Claim 1, which specifically binds to insulin-like growth factor-I receptor (IGF-IR) and comprises at least one complementarity-determining region (CDR) having an amino acid sequence selected from SEQ ID NO:14 at V_HCDR1, SEQ ID NO:16 at V_HCDR2, SEQ ID NO:18 at V_HCDR3, SEQ ID NO:20 at V_LCDR1, SEQ ID NO:22 at V_LCDR2, SEQ ID NO:24 at V_LCDR3, SEQ ID NO:26 at V_LCDR1, SEQ ID NO:28 at V_LCDR2, and SEQ ID NO:30 at V_LCDR3.

13. (Original) The antibody or antigen binding fragment of Claim 1, which comprises SEQ ID NO:14 at V_HCDR1, SEQ ID NO:16 at V_HCDR2, and SEQ ID NO:18 at V_HCDR3.

14. (Original) The antibody or antigen binding fragment of Claim 1, which comprises SEQ ID NO 20 at V_LCDR1, SEQ ID NO:22 at V_LCDR2, and SEQ ID NO:24 at V_LCDR3.

15. (Original) The antibody or antigen binding fragment of Claim 1, which comprises SEQ ID NO 26 at V_LCDR1, SEQ ID NO:28 at V_LCDR2, and SEQ ID NO:30 at V_LCDR3.

16. (Original) The antibody of Claim 1, wherein the heavy chain variable domain has at least 90% sequence homology to SEQ ID NO:2.

17. (Original) The antibody of Claim 1, wherein the light chain variable domain has at least 90% sequence homology to SEQ ID NO:6.

18. (Original) The antibody of Claim 1, wherein the light chain variable domain has at least 90% sequence homology to SEQ ID NO:10.

19. (Original) An isolated nucleic acid encoding a polypeptide selected from the group consisting of:

SEQ ID NO:2 from about amino acid residue 1 to about amino acid residue 130;

SEQ ID NO:6 from about amino acid residue 1 to about amino acid residue 109; and

SEQ ID NO:10 from about amino acid residue 1 to about amino acid residue 109.

20. (Original) The isolated nucleic acid of Claim 19, selected from the group consisting of:

SEQ ID NO:1 from about nucleotide 1 to about nucleotide 390;

SEQ ID NO:5 from about nucleotide 1 to about nucleotide 327; and
SEQ ID NO:9 from about nucleotide 1 to about nucleotide 327.

21. (Original) A recombinant vector comprising a nucleic acid of Claim 19.

22. (Original) A host cell comprising the vector of Claim 21.

23. (Currently Amended) A pharmaceutical composition comprising the antibody or antibody fragment of Claim 1 and a pharmaceutically acceptable carrier.

24. (Currently Amended) A conjugate comprising the antibody or antibody fragment of Claim 1 linked to a cytotoxic agent.

25. (Currently Amended) A conjugate comprising the antibody or antibody fragment of Claim 1 linked to a label.

26. (Currently Amended) A therapeutic composition effective to inhibit growth of human tumor cells that express IGF-IR, which composition comprises the antibody or antigen binding fragment of Claim 1.

27. (Original) The therapeutic composition of Claim 26, which further comprises an anti-neoplastic agent.

28. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

29. (Original) The therapeutic composition of Claim 27, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

30. (Currently Amended) A therapeutic composition effective to promote regression of human tumors that express IGF-IR, which composition comprises the antibody or antibody fragment of Claim 1.

31. (Original) The therapeutic composition of Claim 30, which further comprises an anti-neoplastic agent.

32. (Original) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

33. (Original) The therapeutic composition of Claim 31, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, or etoposide.

34. (Currently Amended) A method of neutralizing the activation of IGF-IR, which comprises administering to a mammal an effective amount of the antibody or antibody fragment of Claim 1.

35. (Currently Amended) A method of treating a proliferative disorder comprising the step of administering an effective amount of the antibody or antibody fragment of Claim 1.

36. (Original) The method of Claim 35, wherein the proliferative disorder is selected from the group consisting of acromegaly, retinal neovascularization, and psoriasis.

37. (Currently Amended) A method of inhibiting the growth of a cell that expresses IGF-IR, which comprises contacting the cell with an effective amount of the antibody or antibody fragment of Claim 1.

38. (Original) The method of Claim 35, which further comprises contacting the cell with an effective amount of an anti-neoplastic agent.

39. (Original) The method of Claim 38, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

40. (Original) The method of Claim 38, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

41. (Currently Amended) A method of reducing tumor growth which comprises administering to a mammal an effective amount of the antibody or antibody fragment of Claim 1.

42. (Original) The method of Claim 41, which further comprises administering an effective amount of an anti-neoplastic agent.

43. (Original) The method of Claim 42, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

44. (Original) The method of Claim 42, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

45. (Currently Amended) A method of promoting tumor regression which comprises administering to a mammal an effective amount of the antibody or antibody fragment of Claim 1.

46. (Original) The method of Claim 45, which further comprises administering an effective amount of an anti-neoplastic agent.

47. (Original) The method of Claim 46, wherein the anti-neoplastic agent is an inhibitor of topoisomerase I or topoisomerase II.

48. (Original) The method of Claim 46, wherein the anti-neoplastic agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

49. (Original) The method of any one of Claims 41 to 48, wherein the tumor is a breast tumor, colorectal tumor, pancreatic tumor, ovarian tumor, lung tumor, prostate tumor, bone or soft tissue sarcoma or myeloma.

50. (Original) A method of inhibiting the growth of a cell that expresses IGF-IR, which comprises contacting the cell with an effective amount of an agent that is an inhibitor of topoisomerase I or topoisomerase II and an antibody or antigen binding fragment thereof that specifically binds to IGF-IR and has at least one property selected from the group consisting of

(i) inhibits binding of IGF-I or IGF-II to IGF-IR;

(ii) neutralizes activation of IGF-IR by IGF-I or IGF-II;

(iii) reduces IGF-IR surface receptor; and

(iv) binds to IGF-IR with a K_d of about 1×10^{-10} M^{-1} or less.

51. (Original) A method of reducing growth of a tumor that expresses IGF-IR, which comprises contacting the cell with an effective amount of an agent that is an inhibitor of topoisomerase I or topoisomerase II and an antibody or antigen binding fragment thereof that specifically binds to IGF-IR and has at least one property selected from the group consisting of

(i) inhibits binding of IGF-I or IGF-II to IGF-IR;

(ii) neutralizes activation of IGF-IR by IGF-I or IGF-II;

(iii) reduces IGF-IR surface receptor by at least about 80%; and

(iv) binds to IGF-IR with a K_d of about 1×10^{-10} M^{-1} or less.

52. (Original) A method of promoting regression of a tumor that expresses IGF-IR, which comprises contacting the cell with an effective amount of an agent that is an inhibitor of topoisomerase I or topoisomerase II and an antibody or antigen binding fragment thereof that specifically binds to IGF-IR and has at least one property selected from the group consisting of

(i) inhibits binding of IGF-I or IGF-II to IGF-IR;

(ii) neutralizes activation of IGF-IR by IGF-I or IGF-II;

(iii) reduces IGF-IR surface receptor by at least about 80%; and

(iv) binds to IGF-IR with a K_d of about 1×10^{-10} M^{-1} or less.

53. (Original) The method of any one of Claims 50 to 52, wherein the agent is selected from the group consisting of irinotecan, camptothecan, and etoposide.

54. (Original) The method of any one of Claims 50 to 52, wherein the antibody or antibody fragment is human.

55. (Original) The method of any one of Claims 50 to 52, wherein the antibody or antibody fragment is humanized.

56. (Original) The method of any one of Claims 51 and 52, wherein the tumor is a breast tumor, colorectal tumor, pancreatic tumor, ovarian tumor, lung tumor, prostate tumor, bone or soft tissue sarcoma or myeloma.